REMARKS

Applicants have carefully studied the Office Action mailed on December 14, 2004, which issued in connection with the above-identified application. The present remarks are intended to be fully responsive to all points of rejection raised by the Examiner and are believed to place the claims in condition for allowance. Favorable reconsideration and allowance of the present claims are respectfully requested.

Pending Claims

Claims 18-34 are pending and at issue in the application. For Examiner's convenience, a list of pending claims is attached as Exhibit A. Claims 18-34 have been rejected under 35 U.S.C. §101 (statutory type double patenting) as claiming the same invention as claims 1-19 of commonly owned U.S. Patent No. 6,596,318. Claims 18, 20-23, 29-32, and 34 have been rejected under 35 U.S.C. §102(b) as being anticipated by WO 97/44015.

35 U.S.C. §101 Rejection

Claims 18-34 have been rejected under 35 U.S.C. §101 (statutory type double patenting) as claiming the same invention as claims 1-19 of a commonly owned U.S. Patent No. 6,596,318 (hereinafter "the '318 patent").

Applicants respectfully traverse the double patenting rejection.

Specifically, applicants note that claims 1-15 of the '318 patent call for a fibrin tissue adhesive formulation containing a mixture of thrombin, and fibrinogen with factor XIII in pourable solid granules, said mixture prepared by: (a) providing solutions or suspensions of the thrombin, and the fibrinogen with factor XIII; (b) drying the solutions in a fluidized bed apparatus; and (c) forming

the pourable solid granules with a particle size of 20-1000 μm. Claims 16-19 of the '318 patent call for a process for producing such fibrin tissue adhesive formulation.

Claims 18-33 of the present application call for a biodegradable depot medicament formulation comprising: (i) a carrier system comprising a biodegradable blood plasma protein, which has been dried by fluidized bed drying with retention of its properties, wherein said blood plasma protein is selected from the group consisting of thrombin, fibrinogen, albumin, and mixtures thereof, and wherein the carrier system is in the form of microporous granules with a particle size in the range from 20 to 500 μm, and (ii) an active ingredient, which is to be administered as a depot or as an active ingredient combination. Claim 34 calls for a process for producing the depot medicament formulation of claim 18.

Accordingly, the scope of the claims of the present application differs from the scope of the claims of the '318 patent in at least two aspects:

(i) while claims of the present application are directed to a biodegradable depot medicament formulation comprising a carrier system and an active ingredient, the claims of the '318 patent are directed to a fibrin tissue adhesive (sealant);

(ii) while claims of the present application encompass formulations comprising both a biodegradable blood plasma protein(s) and an active ingredient, the claims of the '318 patent encompass formulations containing a specific mixture of blood plasma proteins (*i.e.*, thrombin, fibrinogen and factor XIII).

It follows, that, in contrast to the Examiner's assertion, claims 18-34 of the present application are not co-extensive in scope with claims 1-19 of the U.S. Patent No. 6,596,318. Reconsideration and withdrawal of the double patenting rejection is believed to be in order.

35 U.S.C. §102(b) Rejection

In the Office Action, claims 18, 20-23, 29-32, and 34 have been rejected under 35 U.S.C. §102(b) as being anticipated by WO 97/44015. The Examiner contends that "the reference shows particles that are up to 20 microns that read on applicants'" and "further shows other active agents incorporated".

The rejection is respectfully traversed. Specifically, applicants note that claims 18, 20-23 and 29-32 recite microporous granules with a particle size in the range from 20 to 500 μm. In contrast, as acknowledged by the Examiner in section 4 (page 2) of the Office Action, WO 97/44015 "shows particles that are up to 20 microns" (emphasis added). Also, claims 18, 20-23 and 29-32 recite a carrier system comprising a biodegradable blood plasma protein, which has been dried by fluidized bed drying and claim 34 recites a process for producing the depot medicament formulation of claim 18 comprising: (i) spraying the biodegradable blood plasma protein in the form of a solution, or suspension, or both into a fluidized bed installation, and (ii) drying under mild conditions with retention of the properties. In contrast, WO 97/44015 discloses synthesizing fibrin precursor products by spray drying and not by fluidized bed drying (see below). It follows that claims 18, 20-23, 29-32, and 34 are not anticipated by WO 97/44015.

Applicants further respectfully submit that many of the differences between the compositions and methods of WO 97/44015 and the compositions and methods of the present invention (as recited in the present claims) have been discussed during the prosecution of a commonly owned U.S. Patent No. 6,596,318 (hereinafter "the '318 patent"). As noted above, the '318 patent discloses a fibrin tissue adhesive formulation containing pourable solid granules with a particle size of 20-1000 μm prepared by the method which is identical to the method of the present invention, i.e., by drying the solutions in a fluidized bed apparatus. Enclosed for Examiner's review is a Rule 132 Declaration of Professor Peter C. Schmidt submitted during the prosecution of the '318 patent (attached as Exhibit B).

The present claims call for a carrier system comprising a biodegradable blood plasma protein, which has been dried by fluidized bed drying and is in the form of microporous granules

with a particle size in the range from 20 to 500 μm. As explained in detail in Dr. Schmidt's Declaration, by implementing fluidized bed technology, applicants have developed a novel means for producing granules that have advantages over the microparticles of the prior art, particularly of WO 97/44015. WO 97/44015 discloses synthesizing fibrin precursor products by spray drying. As stated at page 3, lines 9-15 and page 8, lines 14-19 of the present application, in contrast to the particles of the present invention produced by fluidized bed drying (which are 20-500 μm and preferably 50-500 μm in size), the spray-dried microparticles disclosed in WO 97/44015 are much smaller (generally 1-20 μm in size; see also page 3, lines 16-18 of WO 97/44015 and sections 6, 11 and 14 of Dr. Schmidt's Declaration) and thus are very prone to dusting and are not free-flowing in practice, which greatly restricts accurate metering and direct application of the solid powder. As specified in sections 7, 11 and 14 and Figure 1 of Dr. Schmidt's Declaration, spray-dried microparticles disclosed in WO 97/44015 are prepared from solution using a pneumatic nozzle which typically produces hollow microspheres which are not free-flowing, difficult to handle (easily crushed), cohesive and cause problems during further processing, transport and storage. In contrast, the larger 20-1000 μm particles produced in a fluidized bed (as are particles of the present application and of the '318 patent) have a slightly porous granule structure, are compact and are not hollow which makes them dust-free, free-flowing, easily metered, rapidly dissolving, and easy to spread (see sections 8, 10, 12 and 14 and Figures 2 and 3 of Dr. Schmidt's Declaration). Also, in contrast to the fluidized bed technology of the present invention which allows to prepare a mixed product containing both fibrinogen and thrombin granules as well as combination granules containing both proteins, the spray drying method disclosed in WO 97/44015 does not allow the fibrinogen and thrombin to be processed together, as their presence together in a liquid solution fed to the dryer would cause a premature reaction -- forming fibrin before it would be of any use to a patient (see page 3, lines 19-20 of WO 97/44015 and sections 5, 7, 9, and 13 of Dr. Schmidt's Declaration).

In sum, the products recited in claims 18, 20-23 and 29-32 and the method recited in claim 34 of the present invention are not the same or an obvious variation of the products and method disclosed in WO 97/44015, due to the differences in particle size, morphology, solubility, dusting and handling properties rendered by the two distinct processes for particle production.

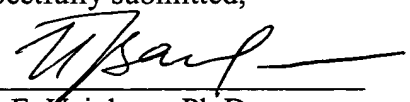
Applicants therefore respectfully submit that WO 97/44015 cited by the Examiner does not anticipate the present claims. Reconsideration and withdrawal of the anticipation rejection is believed to be in order.

CONCLUSION

Applicants request entry of the foregoing remarks in the file history of this application. In view of the above remarks, it is respectfully submitted that pending claims 18-34 are now in condition for allowance and such action is earnestly solicited. If the Examiner believes that a telephone conversation would help advance the prosecution in this case, the Examiner is respectfully requested to call the undersigned agent at (212) 527-7634. The Examiner is hereby authorized to charge any additional fees associated with this response to our Deposit Account No. 04-0100.

Dated: June 7, 2005

Respectfully submitted,

By 

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